Comparison of the Effects of an Adhesion Barrier and Chitin on Experimental Epidural Fibrosis

Deneysel Epidural Fibroziste Adezyon Bariyeri ile Chitin'in Etkinliğinin Karşılaştırılması

ABSTRACT

AIM: Epidural fibrosis is an important factor for postoperative failed back syndrome development and causes clinical complaints in 6-25% of cases. An effective treatment modality has not been found yet. The aim of this study is to investigate the anti-adhesive effects of a novel agent chitin and compare these effects with a popular adhesion barrier collagen matrix.

MATERIAL and METHODS: 21 rabbits were allocated into three groups including 7 rabbits each. L5 total laminectomy was performed to all groups. No treatment was given to Group 1 (Control group). Collagen matrix was used in Group 2 and chitin was used in Group 3. Six weeks later all rabbits were sacrificed and the laminectomy areas were entirely resected and investigated histopathologically.

RESULTS: He and Revel grade III epidural fibrosis was detected in the control group. Statistically significant reduction of epidural fibrosis was achieved with both of the anti-adhesive agents, collagen matrix and chitin, when compared with the control group (p<0.05). The results were not different between treatment groups (p>0.05).

CONCLUSION: The novel agent chitin was found effective for preventing epidural fibrosis and this effect was not significantly different from the collagen matrix. In light of our findings we suggest that chitin is an effective alternative for adhesion barriers.

KEYWORDS: Adhesion barriers, Chitin, Epidural fibrosis

ÖZ

AMAÇ: Başarısız Bel Cerrahisi Sendromunun nedenlerinden biri operasyon sonrası dönemde gelişen epidural fibrozistir ve %6-25 oranında klinik yakınımlara sebep olduğu bildirilmekte olup halen etkili bir tedavi yöntemi bulunamamıştır. Bu çalışmamızda amaç, epidural fibroziste etkinliği bildirilmiş olan kollajen matrix (DuraGen plus) gibi adezyon önleyici madde ile yeni bir ajan olan chitin etkinliğini belirlemek ve karşılaştırmaktır.


BULGULAR: Çalışmamızda kontrol grubunda ortalama grade III epidural fibrozis tespit edildi. Epidural fibrozis çalışma gruptarında kontrol grubuna göre anlamlı olarak düşük bulundu (p<0.05). Tedavi grupları kendi arasında epidural fibrozisi önlemek açısından istatistiksel olarak anlamlı fark tespit edildi (p>0.05).

SONUÇ: Yeni bir ajan olan chitinin epidural fibrozisi önlemeekte etkili olduğu bulundu ve bu etkisi kollajen matriksten farklı olmuştu. Bu bulgular ile chitinin adezyon bariyerleri arasında bir seçeneğe olabileceğini kanaatine varılmıştır.

ANAHTAR SÖZÇÜKLER: Adezyon bariyerleri, Chitin, Epidural fibrozis

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INTRODUCTION

There are many reasons of low back pain and most of them respond to medical treatment. Surgical operation is essential for some of them and a nonhealing low back pain after surgery is a serious problem for the surgeon and patient.

There are also various reasons of postoperative low back pain and fibrosis, which occurs during the physiological wound healing process when it is in excessive amounts and is called epidural fibrosis in spinal surgery (17,18).

Many synthetic and organic materials such as autologous fat grafts, polytetrafluoroethylene membrane, antineoplastic agents, gelfoam, silicone-covered dacron, CO2 laser, vicryl mesh, spongostan, fibrinolytic agents, antiinflammatory agents and dural adhesion have been used to prevent or reduce epidural fibrosis formation. However, so far there is no clinically adopted treatment protocol to prevent epidural fibrosis, (2,6,7,11,20,24,27).

The purpose of our study was to determine the efficacy of novel adhesion barrier chitin (SuproGel) and compare these effects with a well-known adhesion barrier collagen matrix (DuraGen plus).

MATERIAL and METHODS

This study was performed at the Kombassan Experimental and Clinical Research Center of Meram Medical Faculty of Selcuk University, with approval from the local ethic commission. Twenty-one male, white New Zealand rabbits weighing 2500-3000 grams were randomly allocated into three groups. In Group 1 (Control group, n=7), only laminectomy was performed and no treatment was given. In Group 2 (Collagen matrix group, n=7), laminectomy was performed with a collagen matrix patch (DuraGen Plus) applied on dura. In Group 3 (Chitin group, n=7), laminectomy was performed and chitin (SuproGel) injected on the dura. The rabbits were sacrificed six weeks after the surgery. The sacrification process was performed with sodium pentothal solution in 60mg/kg doses (I.E Ulugay, Istanbul-Turkey).

The paravertebral region was exposed and the vertebral column including the paraspinal muscle system was resected in an en bloc fashion with an osteotome.

The tissue samples were fixated with 10% formaldehyde solution for 10 days and decalcified with 90% formic acid. After decalcification, tissue samples were processed to obtain sections of 5 micron thickness. The sections were painted with Hematoxyline-Eosin (H&E) and Masson Trichrome (MT). Preparations were examined on the light microscope by single pathologist in a blind fashion. Fibroblast density, epidural fibrosis, arachnoidal fibrosis and inflammatory cell density were examined (Figure 1,2,3). The histopathological findings were evaluated with He and Revel criteria (12).

Fibroblastic density

Grade 1 : On 400x magnification the fibroblast count is less than 100 in every area

Grade 2 : On 400x magnification the fibroblast count is 100-150 in every area

Grade 3 : On 400x magnification the fibroblast count is more than 150 in every area
Epidural Fibrosis

**Grade 0**: Duramater with no scar formation

**Grade 1**: Existence of only thin fibrous bands between scar tissue and duramater

**Grade 2**: Continuous adhesions filling less than 2/3 of the laminectomy space

**Grade 3**: Adhesions filling more than 2/3 the laminectomy space or spreading to the nerve roots

Arachnoidal Fibrosis

**Grade 0**: undetectable

**Grade 1**: minimal

**Grade 2**: moderate
Grade 3: severe

Inflammatory cell density

Grade 1: On 400x magnification the inflammatory cell count is less than 100 in every area

Grade 2: On 400x magnification the inflammatory cell count is 100-150 in every area

Grade 3: On 400x magnification the inflammatory cell count is more than 150 in every area

Statistical Analysis

The data was analyzed with SPSS 13.0 for Microsoft Windows. The difference between the groups was analyzed with the Kruskal Wallis Variance Analysis Test while the difference between subgroups was analyzed with the Mann Whitney U Test. p<0.05 was accepted as statistically significant.

RESULTS

Control Group:

Grade 3 fibroblastic density was found in 4 rabbits (57.1%), and grade 2 in 3 rabbits (42.9%).

Grade 3 epidural fibrosis was detected in 5 rabbits (71.4%), and grade 2 in 2 (28.6%).

Grade 3 arachnoidal fibrosis was found in 5 rabbits (71.4%), and grade 2 in 2 rabbits (28.6%).

Grade 2 inflammatory cell density was found in 6 rabbits (85.7%), and grade 1 in 1 rabbit (14.3%).

These findings are summarized in Table I.

Collagen Matrix (DuraGen plus) Group:

Grade 2 fibroblastic density was found in 3 rabbits (42.9%), and grade 1 in 4 rabbits (57.1%).

Grade 2 epidural fibrosis was found in 4 rabbits (57.1%), and grade 1 in 3 rabbits (42.9%).

Grade 2 arachnoidal fibrosis was detected in 3 rabbits (42.9%), grade 1 in 3 rabbits (42.9%), and grade 0 in 1 rabbit (14.3%).

Grade 2 inflammatory cell density was found in 2 rabbits (28.6%), grade 1 in 5 rabbits (71.4%).

These findings are summarized in Table II.

After 6 weeks, collagen matrix (DuraGen plus) was completely resorbed in all rabbits

Chitin (SuproGel) Group:

Grade 2 fibroblastic density was found in 1 rabbit (14.5%), and grade 1 in 6 rabbits (85.7%).

Grade 2 epidural fibrosis was found in 2 rabbits (28.6%), and grade 1 in 5 rabbits (71.4%).

Grade 2 arachnoidal fibrosis was found in 1 rabbit (14.3%), grade 1 in 3 rabbits (42.9%), and grade 0 in 3 rabbits (42.9%).

Grade 2 inflammatory cell density was found in 1 rabbit (14.3%), and grade 1 in 6 rabbits (85.7%).

These findings are summarized in Table III.

Chitin (SuproGel) was also completely resorbed 6 weeks after the surgery, without any foreign body reaction.

The collagen matrix (DuraGen plus) and chitin (SuproGel) reduced epidural fibrosis, arachnoidal fibrosis, fibroblastic density and inflammatory cell density. This reduction was statistically significant when compared with the control group (p<0.05). However the difference between the collagen matrix (DuraGen plus) and chitin (SuproGel) group was not statistically significant (p>0.05).

DISCUSSION

Postoperative epidural fibrosis growing on the dural sac and nerve roots causes neurological symptoms and this problem is still waiting a solution in spinal surgery. A relapse of epidural fibrosis in disc surgery is also known to complicate the surgery and increase morbidity (9,14).

Epidural fibrosis is a part of the spinal postoperative healing process. It is seen after almost every operation at a certain rate. It takes the form of an extradural fibrotic structure and adheres to vertebral corpus, anterior disc, posterior erector spina muscles, dura and nerve roots (9).

Epidural fibrosis is one of the accepted causes of failed lumbar surgery syndrome and is responsible for 6 -25% of clinical complaints. There are currently many agents used to prevent epidural fibrosis such as autologous fat grafts, polytetrafluoroethylene membrane, silastic, gelfoam, silicon-coated dacron, CO₂ laser, vicryl mesh, spongostan, fibrolytic agents (plasminogen activator, urokinase), fibrin glue and antiadhesion barrier gel (ADCON-L) which is a polymer of carbohydrate (11,16,23,26,27).

La Rocca et al. stated that the migration of fibroblasts (derived from the erector spina muscles) into the hematoma in the epidural space causes intensive scar formation and epidural fibrosis. Less
surgical dissection and good hemostasis are therefore suggested to decrease scar tissue density (15). Boot and Hughes reported that the laminectomy defect started to close in nearly 4 weeks and scar tissue exactly dissolved in 12 weeks in their research on epidural fibrosis on rabbits (5,25). Some other reports declared that scar tissue formed in less than 8 weeks, confirming this model (2). We performed our study on rabbits in a time period of six weeks.

The basic content of epidural fibrosis is collagen produced by fibroblasts. Barbara et al. reported that collagen was the main substance that was derived
from spinal muscles and filled the laminectomy defect and its quantity was also reported to be proportional with scar tissue (1). We would like to emphasize the collagen density results, especially in the control group, in our study.

Dura rips occur because of the adhesions of epidural fibrosis to the dura, especially in recurrent spinal surgery. A dura graft is also required in traumatic dislocation of bones to the dura and to prevent complications after the surgery of tumors that are adhesive to the dura, such as meningioma (7,21). Dorsal dural defects can be sutured primarily but this is not always possible in lateral and anterior defects. Duragen, having a collagen matrix structure, is used without requiring a suture in those defects and in various disorders encountered in spinal surgery (19). Duragen encompasses fibroblasts thanks to its three-dimensional structure. This infiltration starts on the 3-4th day of the postoperative period and is completed on the 14th day and is then totally resorbed in 6 weeks (10,22). No foreign body reaction was reported in clinical studies and it was also well tolerated immunologically. There was no remnant of duragen plus on histopathological examination in our study consistent with these earlier reports.

SuproGel is an anti-adhesive barrier produced from macromolecular polysaccharide and has a structure similar to human tissue (4,18). It activates cell functions, improves the regeneration of traumatized tissue and provides healing (4). It is currently used as a protecting barrier in abdominal surgery to reduce the intraperitoneal adhesions. Sahin et al. compared SuproGel with other adhesion barriers in a study on rats and they reported that SuproGel was superior in terms of preventing intraabdominal adhesions (24). SuproGel acts as an antiadhesive agent by forming a biological barrier, enhancing epithelial regeneration, preventing fibroblast growth, and decreasing hemorrhage (3). This product is more than just a local adhesion barrier with these additional properties.

In another study on rats, Zeybek et al. reported that SuproGel significantly decreased peritoneal adhesions histopathologically when compared with control group (28). In our study, there were statistically significant differences between the SuproGel group and control group in all parameters. Epidural and arachnoidal fibrosis was also less in the SuproGel group than the DuraGen plus group but this difference was not statistically significant.

In conclusion, all antiadhesive agents reduce post-operative epidural fibrosis. SuproGel, being a new product, can be considered as one of the choices among various adhesion barriers. However, our results require further clinical research for clinical practice.

REFERENCES

10. DuraGen Instructions for Use, Integra Life Sciences Corporation, 1999


22. P. Narotam, A. Gousseau, G. McGinn. Collagen Matrix (DuraGen) for duraplasty following cranial and spinal surgery. 35th. Canadian Congress of Neurological Sciences, Ottawa, Canada, June 2000


